

LISTING OF THE CLAIMS

1. (Original) A method for inducing a biological response in a biological system comprising one or more receptors which comprises the step of introducing into the biological system a multivalent ligand which comprises a plurality of signal recognition elements recognized by at least one of the receptors and bonded to a molecular scaffold.

2.-47. Canceled

48. (Original) The method of claim 1 wherein the multivalent ligand further comprises one or more binding recognition elements, one or more functional elements or both.

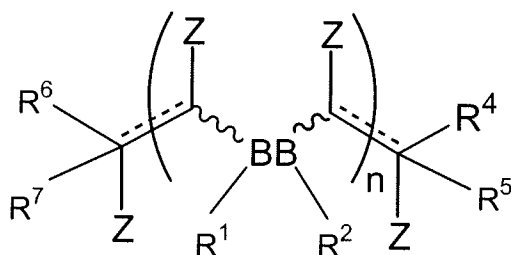
49.-52. Canceled

53. (Original) The method of claim 1 wherein one or more of the signal recognition elements is selected from the group consisting of an amino acid, a peptide, a protein, a derivatized peptide, a monosaccharide, a disaccharide, a polysaccharide, a nucleic acid, a cell nutrient, an epitope, an antigenic determinant, a small drug-like compound, a hapten, an antibody or antibody fragment or a cell surface receptor.

54.-64. Canceled

65. (Original) The method of claim 1 wherein the molecular scaffold is selected from the group consisting of a polyacrylamide, a polyester, a polyether, a polymethacrylate, a polyol, and a polyamino acid.

66. (Original) The method of claim 1 wherein the molecular scaffold is a ROMP polymer.
67. The method of claim 1 wherein the molecular scaffold is an ATRP polymer.
68. (Original) The method of claim 1 wherein the multivalent ligand has the structure:



wherein:

n is an integer that is 2 or more which represents the number of repeating units within the parentheses in the ligand;

the dashed lines indicate optional double bonds;

“BB” represents the backbone repeating unit, which may be cyclic or acyclic, and may be the same or different in a random or block arrangement, the wavy lines indicating that a BB unit may be in either a cis or trans configuration in the ligand backbone;

each R^1 and R^2 , independently of other R^1 and R^2 in the ligand, can be H or an organic group, a recognition element $-L^2\text{-BRE}$, a functional element $-L^3\text{-FE}$ or a signal recognition element $-L^1\text{-SRE}$ or both of R^1 and R^2 can be the $-L^1\text{-SRE}$ group;

wherein L^{1-3} , independently, represent optional linker groups which may be the same or different in different repeating units;

R^4 and R^5 are H, or an organic group;

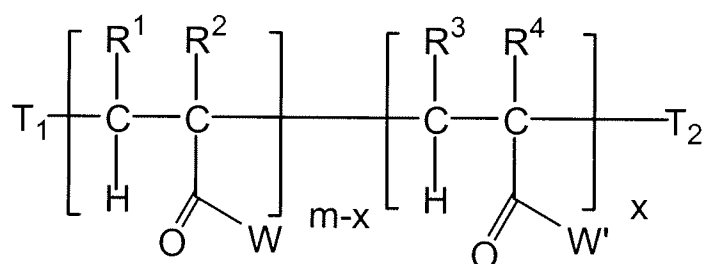
R^6 and R^7 are H, an organic group or an end-group; and

Z, independently of other Z in the ligand, is H, OH, OR⁸, SH, a halide (F, Br, Cl, I), NH₂ or N(R⁸)₂, where R⁸ is H or an organic group or Z is absent when the optional double bond is present.

69. (Original) The method of claim 68 wherein SRE is a peptide or a derivatized peptide, a chemoattractant, a small drug-like compound, an antigen, an epitope, an antibody or antibody fragment

70.-77. Canceled

78. (Original) The method of claim 1 wherein the multivalent-ligand are polymers having the formula:



where:

m and x are integers and m is the number of monomers in the polymer;

W and W' are groups independently selected from -L-BRE, -L-FE, -L-SRE, a hydrogen or an organic group;

L is an optional linker group;

T₁₋₂ are polymer end groups which can include, among others, reactive or non-reactive groups and latent reactive groups; and

R¹⁻⁴ can be the same or different groups and are most generally, independently of one another, hydrogen or any organic groups and where the polymeric ligand contains at least one W or W' that is a BRE or an SRE group.

79. (Original) The method of claim 78 wherein SRE is a peptide or a derivatized peptide, a chemoattractant, a small drug-like compound, an antigen, an epitope, an antibody or antibody fragment.

80.-81. Canceled

82. (Original) The method of claims 78 wherein at least one of SRE is an epitope or antigen and at least one other SRE binds to a cell surface receptor of an immune cell.

83. (Original) The method of claim 78 wherein at least one FE group is a detectable label or a reporter group.

84. (Original) The method of claim 78 wherein an FE in the at least one -L²-FE group in the ligand is an enzyme.

85.-87. Canceled

88. (Original) The method of claim 78 wherein one or more of the BRE, SRE or both are Fab or Fab'.

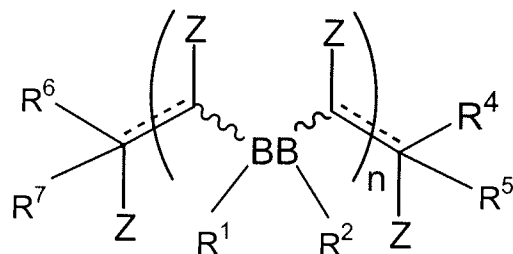
89. (Original) A method for enhancing aggregation of biological particles which comprises the steps of:
providing a multivalent ligand complex which comprises a plurality of recognition elements which each induce aggregation of one or more of the biological particles and contacting the biological particles with the complex.

90. (Original) The method of claim 89 wherein the recognition elements are antibodies or lectins.

91. (Original) The method of claim 89 wherein the biological particles are cells, viruses or virions.
92. (Original) The method of claim 89 wherein the multivalent ligand is a ROMP-derived ligand.
93. (Original) The method of claim 89 wherein the multivalent ligand is an ATRP polymer.
94. Canceled
95. (Currently Amended) A method for inducing or enhancing induction of a cellular response which comprises the steps of:
forming a multivalent ligand which comprises a plurality of signal recognition elements which ~~individually~~ individually bind to the cell and induce the cellular response and contacting the cells with the multivalent ligand in an amount sufficient to enhance the cellular response.
- 96.-98. Canceled
99. (Original) The method of claim 95 wherein one or more of the signal recognition elements are selected from lectins, proteins, nucleic acids, small drug-like compounds, antigens, epitopes, antibodies, antibody fragments, saccharides or mixtures thereof.
100. (Original) The method of claim 95 wherein the multivalent ligand is a ROMP-derived polymer or an ATRP polymer.
101. (Original) A method for generating an assembly of biological macromolecules or particles which comprises the steps of:

- (a) providing a multivalent ligand which comprises a molecular scaffold to which a plurality of binding recognition elements are attached which, in turn, bind to one or more biological macromolecules or biological particles wherein the number, density and spacing of recognition elements bonded to the molecular scaffold are controlled; and
 - (b) contacting the multivalent ligand with biological macromolecules or particles such that the recognition elements of the ligand bind to two or more biological macromolecules or biological particles.
102. (Original) The method of claim 101 wherein the biological macromolecules are peptides or proteins.
103. (Original) The method of claim 101 wherein the biological particles are cells, viruses or virions.
104. (Original) The method of claim 101 wherein the multivalent ligand further comprises one or more FE bonded to the molecular scaffold.
105. (Original) The method of claim 101 wherein the FE is a group that can be attached to a solid support.
106. (Original) The method of claim 101 wherein the members of the assembly of biological macromolecules are attached to a solid support.
107. Canceled
108. (Currently amended) The method of claim 101 wherein the BRE are selected from antibodies, antibody fragments, ~~antigens~~ antigens, or epitopes.

109. (Original) The method of claim 101 wherein the molecular scaffold is a polymer.
110. (Currently amended) A The multivalent ligand of claim 128 having the structure:



wherein:

n is an integer that is 2 or more which represents the number of repeating units within the parentheses in the ligand;

the dashed lines indicate optional double bonds;

“BB” represents the backbone repeating unit, which may be cyclic or acyclic, and may be the same or different in a random or block arrangement, the wavy lines indicating that a BB unit may be in either a cis or trans configuration in the ligand backbone;

each R^1 and R^2 , independently of other R^1 and R^2 in the ligand, can be H or an organic group, a recognition element $-L^2\text{-BRE}$, a functional element $-L^3\text{-FE}$ or a signal recognition element $-L^1\text{-SRE}$ or both of R^1 and R^2 can be the $-L^1\text{-SRE}$ group;

wherein L^{1-3} , independently, represent optional linker groups which may be the same or different in different repeating units;

R^4 and R^5 are H, or an organic group;

R^6 and R^7 are H, an organic group or an end-group; and

Z, independently of other Z in the ligand, is H, OH, OR⁸, SH, a halide (F, Br, Cl, I), NH₂ or N(R⁸)₂, where R⁸ is H or an organic group or Z is absent when the optional double bond is present.

111. (Original) The multivalent ligand of claim 110 wherein BRE, SRE or both are selected from the groups peptides, derivatized peptides, proteins, cell-surface receptors, saccharides, lectins, nucleic acids, antibodies, antibody fragments, antigens, epitopes, cells, viruses, and virions.

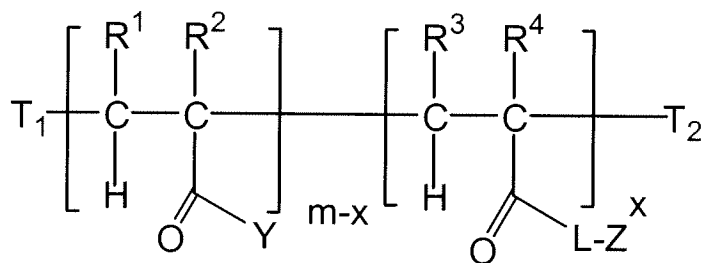
112.-115. Canceled

116. (Original) The multivalent ligand of claim 110 wherein at least one SRE or BRE is a recognition molecule selected from the group consisting of Fab, Fab', scFv and scFv-hybrid.

117. (Currently amended) The multivalent ligand of claim 116 which comprises at least two recognition molecules of different specificities.[[.]]

118. Canceled.

119. (Currently amended) The A multivalent ligand of claim 128 having the formula:



where:

m and x are integers, x is the number of monomers carrying a Z group and m is the number of monomers in the polymer; the structure of the above

formula reflects the relative number, but does not reflect the relative positions of Y and Z groups in the polymer;

Z is a metal chelating group or a metal chelating group chelated to one or more metal species;

Y is a chemical group that is not a metal chelating group, which more specifically can be selected from any organic group, an $-L^2$ -BRE group, an $-L^3$ -FE group, or an $-L^1$ -SRE;

T_{1-2} are polymer end groups which can include, among others, reactive or non-reactive groups and latent reactive groups;

L and L^{1-3} are optional linker groups; and

R^{1-4} can be the same or different groups and are most generally, independently of one another, hydrogen or any organic groups, or more particularly hydrogen or any hydrocarbyl groups, as well as hydrocarbyl groups substituted with one or more heteroatoms, one or more halogens, one or more $-SR^5$ groups, one or more $-OR^5$ groups, where R^5 is a hydrogen or any organic groups, including hydrocarbyl groups and substituted hydrocarbyl groups, one or more amine groups $-N(R^5)^2$ where R^5 , independent of other R^5 groups is a hydrogen, or any organic groups again including any hydrocarbyl or substituted hydrocarbyl groups, or one or more halogen groups.

120. (Original) The multivalent ligand of claim 119 wherein BRE, SRE or both are selected from the groups peptides, derivatized peptides, proteins, cell-surface receptors, saccharides, lectins, nucleic acids, small drug-like compounds, antibodies, antibody fragments, antigens, epitopes, cells, viruses, and virions.
121. (Original) The multivalent ligand of claim 119 wherein FE are reporter groups or labels.

122. Canceled
123. (Original) The multivalent ligand of claim 119 which comprises at least two different SRE.
124. (Original) The multivalent ligand of claim 119 which comprises at least one BRE and at least one SRE.
125. (Original) The multivalent ligand of claim 119 wherein at least one SRE or BRE is a recognition molecule selected from the group consisting of Fab, Fab', scFv and scFv-hybrid.
126. (Original) The multivalent ligand of claim 119 which comprises at least two recognition molecules of different specificities.
127. Canceled
128. (New) A multivalent ligand comprising a plurality of signal recognition elements recognized by at least one receptor on an erythrocyte and bonded to a molecular scaffold which is a polymer.
129. (New) The multivalent ligand of claim 128 wherein the molecular scaffold is selected from the group consisting of a polyacrylamide, a polyester, a polyether, a polymethacrylate, a polyol, and a polyamino acid.
130. (New) The multivalent ligand of claim 128 wherein the polymer is a linear polymer.
131. (New) The multivalent ligand of claim 128 wherein the polymer is a ROMP-derived polymer or an ATRP polymer.

132. (New) The multivalent ligand of claim 128 wherein the signal recognition elements are covalently bonded to the polymer.
133. (New) The multivalent ligand of claim 128 wherein the signal recognition elements are noncovalently bonded to the molecular scaffold.
134. (New) The multivalent ligand of claim 128 wherein the multivalent ligand comprises about 25 or more signal recognition elements .
135. (New) The multivalent ligand of claim 128 wherein the multivalent ligand comprises about 100 or more signal recognition elements.
136. (New) The multivalent ligand of claim 128 which is bonded to a solid support.
137. (New) The multivalent ligand of claim 136 further comprising binding recognition elements that selectively bind to an antigen or pathogen.
138. (New) The multivalent ligand of claim 136 wherein the binding recognition elements are antibodies or fragments thereof.
139. (New) The multivalent ligand of claim 119 which does not carry a metal chelating group.
140. (New) The multivalent ligand of claim 139 wherein Y is selected from an organic group, an $-L^2$ -BRE group, an $-L^3$ -FE group, or an $-L^1$ -SRE.
141. (New) The multivalent ligand of claim 140 wherein BRE and SRE are selected from antibodies or fragments thereof.

142. (New) The multivalent ligand of claim 141 wherein SRE and BRE are recognition molecules selected from the group consisting of Fab, Fab', scFv and scFv-hybrids.
143. (New) The multivalent ligand of claim 142 wherein SRE and BRE are both Fab'.
144. (New) The multivalent ligand of claim 143 wherein SRE is a Fab' fragment having specificity for a receptor on erythrocytes.
145. (New) The multivalent ligand of claim 144 wherein SRE is an anti-CR1 Fab'.
146. (New) The multivalent ligand of claim 143 wherein BRE is a Fab' fragment having specificity for a selected pathogen.
147. (New) The multivalent ligand of claim 146 wherein BRE is a Fab' fragment having specificity for a pathogen selected from a fungal, protozoan, bacterial or viral pathogen.
148. (New) The multivalent ligand of claim 147 wherein BRE is a Fab' fragment for a bacterium.
149. (New) The method of claim 1 wherein the biological response is immune adherence and the biological system comprises erythrocytes.
150. (New) The method of claim 149 wherein the receptor is a receptor on the erythrocytes.
151. (New) The method of claim 150 wherein the receptor is CR1.

152. (New) The method of claim 150 wherein the signal recognition element is an antibody or fragment thereof which is selective for the receptor on the erythrocytes.
153. (New) The method of claim 152 wherein the receptor is CR1.
154. (New) The method of claim 153 wherein the signal recognition element is a Fab' fragment.
155. (New) The method of claim 154 wherein the multivalent ligand further comprises an antibody or fragment thereof which selectively binds to the pathogen.
156. (New) The method of claim 155 wherein the antibody or fragment thereof is a Fab' fragment.
157. (New) The method of claim 101 wherein the biological macromolecules or particles are antigens or pathogens.
158. (New) The method of claim 157 wherein the biological particles are pathogens.
159. (New) The method of claim 158 wherein the pathogens are selected from the group of fungal, protozoan, bacterial or viral pathogens.
160. (New) The method of claim 150 wherein the pathogen is a bacterial pathogen.

161. (New) The method of claim 101 wherein the multivalent ligand comprises binding recognition elements selectively bind to a pathogen.
162. (New) The method of claim 161 wherein the multivalent ligand further comprises signal recognition elements which bind to a receptor on erythrocytes.
163. (New) The method of claim 162 wherein the signal recognition elements are antibodies or fragments thereof.
164. (New) The method of claim 162 wherein the signal recognition elements are Fab, Fab', scFv and scFv-hybrids.
165. (New) The method of claim 164 wherein the signal recognition elements are Fab' fragments.
166. (New) The method of claim 157 wherein the polymer is an ATRP polymer or a ROMP polymer.
167. (New) The method of claim 166 wherein the polymer is an ATRP polymer.
168. (New) The method of claim 157 wherein the polymer is selected from a polyacrylamide, a polyester, a polyether, a polymethacrylate, a polyol, and a polyamino acid.
169. (New) The method of claim 157 wherein the polymer is selected from a polyacrylamide, a polyester, a polyether, a polymethacrylate, and a polyol.
170. (New) The method of claim 169 wherein the polymer is a polymethacrylate.

171. (New) The method of claim 170 wherein the polymer comprises a signal recognition element that binds to a receptor on an erythrocyte.
172. (New) The method of claim 171 wherein the polymer further comprises a binding recognition element that binds selectively to a pathogen or an antigen.
173. (New) The method of claim 172 wherein the signal recognition element and the binding recognition element are both antibody fragments.
174. (New) The method of claim 173 wherein the antibody fragments are Fab' fragments.
175. (New) The method of claim 174 wherein the binding recognition element binds to a selected pathogen.
176. (New) The method of claim 175 wherein the pathogen is a fungal, protozoan, bacterial or viral pathogen.
177. (New) The method of claim 176 wherein the pathogen is a bacterial pathogen.